REMARKS

Pending claims 1-8, 11-20, 27 and 29 were rejected. Claim 2 was canceled as being redundant to the claims as amended. Claims 9-10, 21-26, 28, and 30-40 were withdrawn from consideration. Claims 41-53 were added and claims 1-8, 11-20, 27 and 29 were amended to more accurately point out that the applicants regard as their invention. Specifically, the claims were amended to provide that the protein free medium "comprises an oncotic agent". Support may be found in the specification generally and on page 4, lines 9-15, page 6, lines 17 to page 7, line 3, and page 9, lines 11-13. Additionally, the claims were amended to indicate that the soluble antigen is obtained "by culturing the Leishmania parasite" in the protein free medium comprising the oncotic agent. Support may be found in the specification generally, and specifically in the detailed examples. No statutory new matter has been added. Therefore, the Applicants respectfully request that the amendment be entered.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 1-8 under 35 U.S.C. 112, first paragraph, as the Examiner deemed that an immunoassay for detecting leishmaniasis in a subject by detecting or measuring an antibody *fragment* bound to the soluble antigen is not enabled.

Applicants respectfully assert that the detection of antibody fragments in a sample obtained from a subject is enabled by the disclosure of the present application and may be practiced by using conventional methods in the art. Although antibody fragments are not generally in a sample obtained from a subject where the sample is not exposed to proteolytic enzymes, it is possible by conventional methods in the art to, as the Examiner accurately pointed out, expose the sample to papain or trypsin in order to cleave the immunoglobulin molecule into fragments. The Examiner also accurately pointed out that cleaving an antibody may affect its antigen binding specificity and affinity.

However, Applicants respectfully assert that screening a sample and detecting whether an antibody fragment of an immunoglobulin molecule against a leishmanial soluble antigen is enabled by the disclosure of the present application by conventional methods and routine screening. Specifically, one of ordinary skill in the art would be able practice the present invention as claimed, by obtaining a sample from a subject, exposing the sample to proteolytic

enzymes and then screening the sample for antibody fragments which bind to the soluble antigen. Routine screening methods are not undue experimentation. See *Ex parte Mark*, 12 U.S.P.Q.2d 1904 (Bd. App. 1989).

In order to detect antibody fragments in the sample, one need only expose the sample to proteolytic enzymes and then screen the samples for activity, i.e. specificity and binding by methods set forth in the specification and conventional assay methods. Thus, the claims are fully enabled, and the rejection under 35 U.S.C. 112, first paragraph, may be properly withdrawn.

The Examiner also rejected the claims under 35 U.S.C. 112, first paragraph, for lack of enabling disclosure, as the Examiner deemed that detection of an "unknown soluble antigen require undue experimentation". The Examiner then cited Martin *et al.* for evidence that "an immunoassay ... utilizing soluble antigens from an unknown source requires further experimentation".

It is unclear to the Applicants how Martin *et al.* supports the assertion that undue experimentation is required. Especially, in light of the fact that the Examiner is asserting Martin *et al.* as an anticipatory reference. However, as explained in detail below, Martin *et al.* may not be used as a prior art reference as it does not provide an enabling disclosure.

Nevertheless, Applicants respectfully assert that immunoassays for *any soluble antigen* obtained from a protein free medium are enabled as one of ordinary skill in the art need only practice the invention as disclosed. A person need not know the details or specifics about the source, i.e. the *Leishmania* parasite strain, the amino acid sequence, and other information about the particular soluble antigens excreted by the *Leishmania* parasite. Herein lies the beauty and simplicity of the invention as one of ordinary skill in the art is able to practice the invention as claimed and disclosed by merely using the unknown or uncharacterized soluble antigen obtained from culturing any *Leishmania* parasite in the protein free medium comprising an oncotic agent and then detecting whether a subject has antibodies against the antigen.

As the claims as amended are enabled, the rejection under 35 U.S.C. 112, first paragraph, may be properly removed.

Rejection under 35 U.S.C. 102(b)

The Examiner rejected claims 1-5, 7 and 8 as being anticipated by Martin *et al.*

Applicants respectfully assert that the claims as amended are not anticipated by Martin *et al.* Specifically, in order to anticipate, the reference must provide an enabling disclosure and teach each and every element of the claim. See MPEP 2121 and MPEP 2131.

Applicants respectfully assert that even though Martin *et al.* discloses that a protein free medium, XOM, was used to obtain the antigen used in the immunoassay, Martin *et al.* does not enable the immunoassays disclosed in Martin *et al.* and the present specification. Specifically, Martin *et al.* never disclosed the oncotic agent that balances the oncotic pressure across the semipermeable membrane of the parasite. Additionally, XOM is not available to general public, those without permission from the inventors, as GIBCO is under a strict agreement to not disclose the ingredients of XOM or make it available to others.

An oncotic agent must be present in the protein free medium used to culture the parasites or else, the parasites will die. The prior art media used to culture organisms all comprise protein which acts as an agent to balance the oncotic pressure which allows the organisms to survive. Previous attempts by others have been made to create a protein free medium to culture certain organisms, however, such attempts were unsuccessful.

Thus, Martin *et al.* is a nonenabling disclosure as neither XOM nor its ingredients were disclosed or made available to others and knowledge and use of *a protein free medium comprising an oncotic agent*, such as xylose, is necessary in order to practice the present invention. Therefore, Martin *et al.* is not an enabling prior art reference and may not be used to anticipate the present invention as claimed. Additionally, as the prior art does not teach or disclose the oncotic agent, the claims as amended are not anticipated. Therefore, the rejection under 35 U.S.C. 102(b) may be properly withdrawn.

Rejection under 35 U.S.C. 103(a)

The Examiner rejected the claims under 35 U.S.C. 103(a) as being obvious over Martin *et al.* in view of Wirtz *et al.* and WO 99/56755.

Applicants respectfully assert that a prima facie case of obvious has not been established. Specifically, the invention as a whole was not taught, disclosed, or suggested by the prior art references. In particular, the use of an oncotic agent in order to practice the invention is not taught, disclosed or suggested anywhere in Martin *et al.*, Wirtz *et al.* or WO 99/56755, or any other reference in the prior art.

The prior art immunoassays have suffered from problems relating to the inability to obtain a pure antigen solely from a given organism. The inability to obtain a pure antigen is due to the fact that an oncotic agent must be present in the media used to culture the organism, and, prior to the present invention, no one in the art understood this to be true. All that was known was that when a completely protein free medium was used, the organisms died. Thus, those skilled in the art always added a protein such as albumin. However, the proteins that are added may contaminate the antigen secreted into the medium. Additionally, the proteins added may be metabolized. When antibodies prepared against such antigenic preparations are used, the antibodies have undesired reactivity against the added proteins and metabolites thereof. Thus, nowhere in the prior art is the use of a soluble antigen obtained from using a protein free medium comprising an oncotic agent taught, disclosed or suggested for using in an immunoassay with a reasonable expectation of success by one of ordinary skill in the art.

As none of the disclosures of the cited references, alone or in combination, teach, disclose, or suggest each and every limitation of the invention as claimed, the rejection under 35 U.S.C. 103(a) may be properly withdrawn.

Objections

Applicants note the objections to the drawings and upon a notice of allowance the Applicants will submit formal drawings.

Applicants note that the term "fragment" does not have antecedent basis in the specification. Therefore, upon an indication of allowable subject matter, Applicants will provide an amended Specification.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. **210380**, referencing Attorney Docket No. **P66748US1 (WRAIR 98-41X).**

Attached hereto is a marked-up version of the changes made by the present amendment entitled "**Version with Markings to Show Changes Made**."

Respectfully submitted,
JACOBSON HOLMAN, PLLC

Suzannah K. Sundby
Reg. No. 43,172

Date: 28 July 2001
The Jenifer Building
400 Seventh Street, N.W.
Washington, DC 20004-2201
(202) 662-8497